CLAIMS

1. A method of screening for small organic molecules that directly inhibit the interaction of glycosaminoglycans (GAGs) with GAG-binding viral proteins (GBVPs), the method comprising the steps of:

(a) contacting a GAG with an GBVP in the presence of at least one candidate compound; and

(b) measuring the amount of the GAG bound to the GBVP or the amount of the GBVP bound to the GAG, wherein a significant decrease in GAG-GBVP binding as compared to GAG-GBVP binding in the absence of the candidate compound, identifies said compound as inhibitor of the GAG-GBVP interaction.

2. A method of screening for small organic compounds that directly inhibit the interaction of glycosaminoglycans (GAGs) with GAG-binding viral proteins (GBVPs), the method comprising the steps of:

(a) contacting a GAG with at least one candidate small organic compound;

(b) removing unbound organic compound;

(c) adding a GBVP; and

(d) measuring the amount of the GAG bound to the GBVP or the amount of the GBVP bound to the GAG, wherein a significant decrease in GAG-GBVP binding as compared to GAG-GBVP binding in the absence of the candidate compound, identifies said compound as inhibitor of the GAG-GBVP interaction

3. The method according to claim 1 or 2, wherein the GBVP is a fusion protein.

4. The method according to claim 1 or 2, wherein the GAG or the GBVP is tagged or labeled.

5. The method according to claim 1 or 2, wherein the GAG is heparan sulfate (HS-GAG) or heparin.

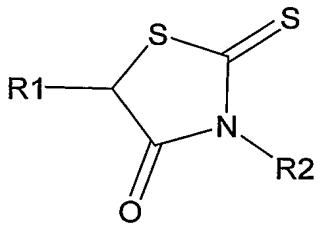
6. The method according to claim 1 or 2, wherein the small organic molecules are contacted with a proteoglycan containing GAG.

7. A method for the treatment or prevention of disorders related to virus attachment and entry or to bacterial or parasite attachment, comprising the step of administering to a subject in need thereof a therapeutically effective amount of a compound that directly inhibits the interaction of glycosaminoglycans (GAGs) with GAG-binding viral proteins (GBVPs), thus preventing virus attachment and entry or bacterial or parasite attachment mediated by the GAG.

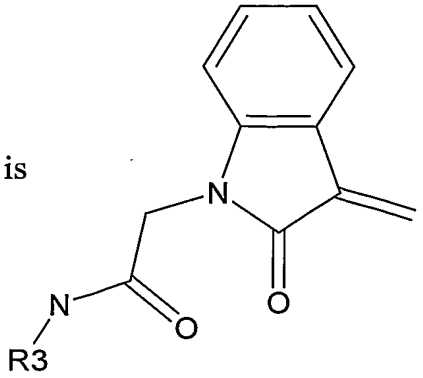
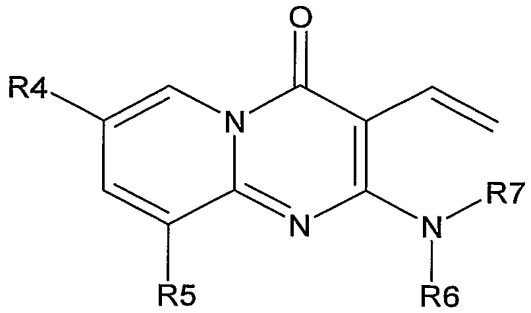
8. The method according to claim 7, wherein the disorder related to virus attachment and entry is an infection caused by a virus selected from the group consisting of a HIV, a HSV, CMV, HCV, RSV, an influenza virus, and rhinovirus.

9. The method according to claim 7, wherein the disorder related to bacterial or parasite attachment is a bacterial infection or a parasite-induced disease such as malaria.

10. A pharmaceutical composition comprising a pharmaceutically acceptable diluent or carrier and an active ingredient of the general formula I:



wherein

R1 is  or  ;

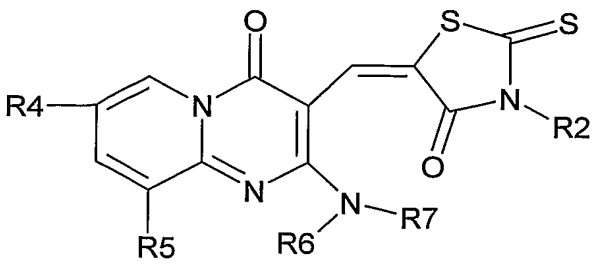
R2 is C_1-C_6 alkyl unsubstituted or substituted by a radical selected from the group consisting of $-SO_3H$, C_1–C_6 alkoxy, phenyl, 4-(C_1–C_6)alkylphenyl, 4-(C_1–C_6)alkoxyphenyl, 2-furyl, tetrahydro-2-furyl, or 1,3-benzodioxinyl, or R_5 is cycloalkyl or C_2-C_6 alkenyl;

R3 is phenyl substituted by at least one radical selected from the group consisting of C_1-C_6 alkyl, hydroxy(C_1-C_6)alkyl, C_1-C_6 alkoxy, cyano, halogen, trifluoromethyl, cycloalkyl, aralkyl, aryl, substituted aryl, and heterocyclyl;

R4 and R5 each is hydrogen or C_1-C_6 alkyl;

R6 and R7 each is selected from the group consisting of C_1–C_6 alkyl, C_1–C_6 alkyl substituted by piperidinyl, 4-morpholinyl, piperazinyl, 4-(C_1–C_6)alkyl-piperazinyl, 4-arylpiperazinyl, 4-aralkylpiperazinyl, or imidazolyl; C_3–C_7 cycloalkyl, C_6–C_{10} aryl, C_7–C_{16} aralkyl, and C_7–C_{16} aralkyl, or R_3 and R_4 together with the nitrogen atom to which they are attached form a 5 to 7 membered saturated heterocyclic ring containing one or two heteroatoms and optionally substituted at the additional nitrogen atom by C_1–C_6 alkyl optionally substituted by halogen, hydroxyl, C_1–C_6 alkoxy or phenyl, or C_2–C_7 alkoxycarbonyl, and pharmaceutically acceptable salts thereof.

11. The pharmaceutical composition according to claim 10, comprising a compound of the general formula Ia:



Ia

wherein:

R2 is C_1-C_6 alkyl unsubstituted or substituted by C_1–C_6 alkoxy, phenyl, 4-(C_1–C_6)alkylphenyl, 4-(C_1–C_6)alkoxyphenyl, 2-furyl, tetrahydro-2-furyl, or 1,3-benzodioxinyl, or R_5 is cycloalkyl or alkenyl;

R4 and R5 each is hydrogen or C_1-C_6 alkyl;

R6 and R7 each is selected from the group consisting of C_1–C_6 alkyl, C_1–C_6 alkyl substituted by piperidinyl, 4-morpholinyl, piperazinyl, 4-(C_1–C_6)alkyl-piperazinyl, 4-arylpiperazinyl, 4-aralkylpiperazinyl, or imidazolyl; C_3–C_7 cycloalkyl, C_6–C_{10} aryl, C_7–C_{16} aralkyl, and C_7–C_{16} aralkyl, or R_3 and R_4 together with the nitrogen atom to which they are attached form a 5 to 7 membered saturated heterocyclic ring containing one or two heteroatoms and optionally substituted at the additional nitrogen atom by C_1–C_6 alkyl optionally substituted by halogen, hydroxyl, C_1–C_6 alkoxy or phenyl, or C_2–C_7 alkoxycarbonyl,

and pharmaceutically acceptable salts thereof.

12. The pharmaceutical composition according to claim 11, wherein the compound of formula Ia is selected from the group consisting of:

4H-Pyrido[1,2-a]pyrimidin-4-one, 3-[[3-[(2-methylpropyl)methyl)] -4-oxo-2-thioxo-5-thiazolidinylidene]methyl]-2-[4-(2-hydroxyethyl)-1-piperazinyl]- (Compound **1**)

4H-Pyrido[1,2-a]pyrimidin-4-one, 3-[[3-(phenylethyl)-4-oxo-2-thioxo-5-thiazolidinylidene]methyl]-2-[[2-(4-morpholinyl)ethyl]amino]-9-methyl- (Compound **2**)

4H-Pyrido[1,2-a]pyrimidin-4-one, 3-[(3-pentyl -4-oxo-2-thioxo-5-thiazolidinylidene)methyl]-2-(4-methyl-1-piperazinyl)- (Compound **3**)

4H-Pyrido[1,2-a]pyrimidin-4-one, 3-[[3-(phenymlethyl)-)-4-oxo-2-thioxo-5-thiazolidinylidene]methyl]-2-(4-methyl-1-piperazinyl)- (Compound **4**)

4H-Pyrido[1,2-a]pyrimidin-4-one, 3-[(3-phenylmethyl-4-oxo-2-thioxo-5-thiazolidinylidene)methyl]-2-(4-methyl-1-piperazinyl)- 7-methyl- (Compound **5**)

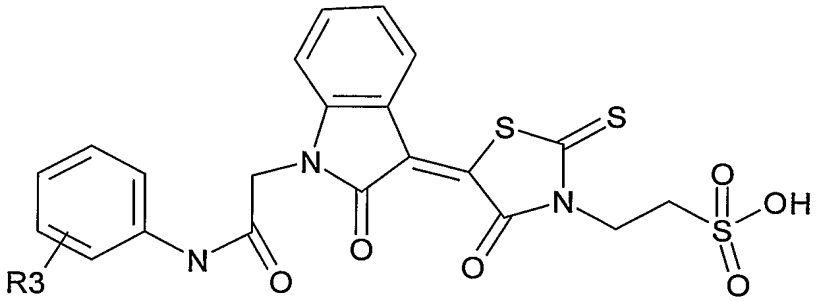
4H-Pyrido[1,2-a]pyrimidin-4-one, 3-[[3-[(4-methoxyphenyl)methyl] -4-oxo-2-thioxo-5-thiazolidinylidene]methyl]-2-(4-methyl-1-piperazinyl)- (Compound **6**)

4H-Pyrido[1,2-a]pyrimidin-4-one, 3-[(3-butyl-4-oxo-2-thioxo-5-thiazolidinylidene)methyl]-9-methyl-2-(4-methyl-1-piperazinyl)- (Compound **10**)

4H-Pyrido[1,2-a]pyrimidin-4-one, 3-[(3-phenylmethyl-4-oxo-2-thioxo-5-thiazolidinylidene)methyl]-2-[[3-(1H-imidazol-1-yl)propyl]amino]-(Compound **25**)

4H-Pyrido[1,2-a]pyrimidin-4-one, 3-[[3-(phenylmethyl)-4-oxo-2-thioxo-5-thiazolidinylidene]methyl]-2-[[2-(4-morpholinyl)ethyl]amino]-9-methyl- (Compound **26**).

13. The pharmaceutical composition according to claim 10, comprising a compound of the general formula Ib:



Ib

wherein:

R3 is C_1-C_{10} alkyl, hydroxy(C_1-C_{10})alkyl, C_1-C_6 alkoxy, cyano, halogen, trifluoromethyl, cycloalkyl, aralkyl, aryl, substituted aryl, and heterocyclyl;

and pharmaceutically acceptable salts thereof.

14. The pharmaceutical composition according to claim 13, wherein R3 is methyl, ethyl, hydroxyethyl, halogen, cyano, 3,4-dicyano, methoxy, 4,5-dimethoxy, or 3-trifluoromethyl.

15. The pharmaceutical composition according to claim 13, wherein the compound of formula Ib is:

5-[1,2-dihydro-2-oxo-1-[2-oxo-2-[[3-(trifluoromethyl)phenyl]amino]ethyl]-3H-indol-3-ylidene]-4-oxo-2-thioxo-3-thiazolidineethanesulfonic acid [**Compound 11**]; or

5-[1,2-dihydro-2-oxo-1-[2-oxo-2-[3-(cyanophenyl)amino]ethyl]-3H-indol-3-ylidene]-4-oxo-2-thioxo-3-thiazolidineethanesulfonic acid.

16. The pharmaceutical composition according to any of claims 10 to 15, for treatment or prevention of viral diseases, disorders or conditions mediated by virus-to-cell attachment via heparan sulfate glycosaminoglycans (HS-GAGs).

17. The pharmaceutical composition according to claim 16, wherein the viral disease is an infection caused by a virus selected from the group consisting of a HIV, a HSV, CMV, HCV, RSV, an influenza virus, and rhinovirus.

18. The pharmaceutical composition according to any of claims 10 to 15, for treatment or prevention of disorders mediated by bacteria-to-cell or parasite-to-cell attachment via heparan sulfate glycosaminoglycans (HS-GAGs).

19. Use of a compound of the general formula I in claim 10 for the preparation of a pharmaceutical composition.

20. The use according to claim 19, wherein the pharmaceutical composition is for treatment or prevention of viral diseases, disorders or conditions mediated by virus-to-cell attachment via heparan sulfate glycosaminoglycans (HS-GAGs).

21. The use according to claim 20, wherein the viral disease is an infection caused by a virus selected from the group consisting of a HIV, a HSV, CMV, HCV, RSV, an influenza virus, and rhinovirus.

22. A method for the treatment or prevention of viral diseases, disorders or conditions mediated by virus-to-cell attachment via heparan sulfate glycosaminoglycans (HS-GAGs), comprising the step of administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a compound of the general formula I in claim 10.

23. The method according claim 22, wherein the viral disease is selected from a group consisting of HIV, HSV, CMV, HCV, RSV, influenza virus, and rhinovirus infection.